Willem P.C. Stemmer

Application No: 10/623,036

Filed: July 18, 2003

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## Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application.

## **Listing of Claims:**

- 1. (Previously presented) A method for selecting or screening a library of recombinant proteins to identify a recombinant protein having a desired functional property, said method comprising:
- a) randomly fragmenting a template double-stranded DNA into a plurality of double-stranded fragments of a desired size;
- b) adding to the resultant population of double-stranded fragments one or more single or double-stranded oligonucleotides, wherein said oligonucleotides comprise an area of identity and an area of heterology to the template polynucleotide;
- c) denaturing the resultant mixture of double-stranded random fragments and oligonucleotides into single-stranded fragments;
- d) incubating the resultant population of single-stranded fragments with a polymerase under conditions which result in the annealing of said single-stranded fragments at regions of identity, to form pairs of annealed fragments, said areas of identity being sufficient for one member of a pair to prime replication of the other thereby forming mutagenized double-stranded DNA molecules;
- e) repeating steps (c) and (d) a desired number of times, wherein repeated step c) comprises denaturing the mutagenized double-stranded DNA molecules from step d) of the previous cycle to form a library of mutagnized double-stranded DNA molecules;
- f) expressing a library of recombinant proteins from the library of mutagenized double-stranded DNA from step e); and
- g) selecting or screening the library of recombinant proteins to identify a recombinant protein with a desired functional property.
- 2. (Original) The method of Claim 1 wherein the concentration of a specific double-stranded fragment in the mixture of double-stranded fragments is less than 1% by weight of the total DNA.

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- 3. (Original) The method of Claim 1 wherein the number of different specific double-stranded fragments comprises at least about 100.
- 4. (Original) The method of Claim 1 wherein the size of the double-stranded fragments is from about 5 bp to 5 kb.
- 5. (Previously presented) The method of Claim 1 wherein the size of the mutagenized double-stranded DNA molecules in the library of mutagenized double-stranded DNA molecules is from about 50 bp to 100 kb.

Claims 6-32 (Cancelled)

- 33. (Previously presented) The method of Claim 1, wherein the template double-stranded polynucleotide encodes a wild-type protein.
- 34. (Previously presented) The method of Claim 1, wherein the polymerase is Taq.
- 35. (Previously presented) The method of Claim 1, wherein the polymerase is Klenow polymerase.
- 36. (Previously presented) The method of Claim 1, wherein the template double-stranded DNA is from 50 bp to 50 kb.
- 37. (Previously presented) The method of Claim 1, wherein the size of the double-stranded fragments is from about 10 bp to 1000 bp.
- 38. (Previously presented) The method of Claim 1, wherein the size of the double-stranded fragments is from about 20 bp to 500 bp.
- 39. (New) The method of Claim 1, wherein the template double-stranded DNA in step a) is obtained from DNA associated with a displayed antibody that has been screened for affinity for binding a predetermined ligand, and wherein the library of recombinant proteins in step f) is expressed as an antibody display library.